

PATENT
 USSN 10/044,692
 TTC Docket 002640US
 Geron Docket 018/213c

REMARKS

This paper is responsive to the Office Action dated April 21, 2005, which is the first action on the merits of the application.

Claims 1 and 10-38 were previously pending in the application, of which 1, 10 and 19-33 were under examination. Upon entry of this paper into the file, claims 11-18 and 34-38 are cancelled, and new claims 39-54 are introduced to replace the cancelled claims. The new claims come within the group under examination.

Accordingly, claims 1, 10, 19-33, and 39-54 are now pending and under examination. Further consideration and allowance of the application is respectfully requested.

Interview summary:

The undersigned wishes to express his appreciation to Examiner Ungar for very productive telephone consultations on September 15 and October 25. Suitable claim wording and support for the claim wording in the specification were discussed.

The amendments and remarks made in this submission are believed to clear up all issues in the case, and a notice of allowance is respectfully requested.

Amendments

Entry of the claim amendments does not introduce new matter into the disclosure. Support for the claim as amended here may be found throughout the specification and the claims as previously presented. The amendments are made to obtain coverage for certain aspects of the invention that are of current commercial interest. Applicant reserves the right to introduce claims to subject matter previously claimed or described in the disclosure in this or any other application.

Insofar as it relates to nucleic acids of this invention, parts b), and c) of claim 1 have been reworded without introducing any substantial new limitation. Some of the dependent claims (e.g., claims 29-32) have also been amended in a manner that does not introduce further limitations. Accordingly, coverage is maintained for all equivalents of the subject matter in these claims for which applicant was previously entitled.

Claim 1 and its dependents invoke a nucleic acid that encodes hTERT or a polypeptide consisting of at least 20 contiguous amino acids of SEQ. ID NO:2. The skilled reader will understand

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this to mean that the polypeptide will contain 20 and potentially more consecutive amino acids from the hTERT sequence.

Claims 21, 23, 24, 43, and their dependents cover a composition comprising a nucleic acid encoding a polypeptide fragment *consisting essentially of at least 10, 20, or 50 contiguous amino acids of SEQ. ID NO:2 which is immunogenic for a specific response against hTERT (SEQ. ID NO:2)*. This means that the polypeptide fragment contains said 10, 20, or 50 or more contiguous amino acids of SEQ. ID NO:2, and may optionally contain additional amino acid(s) at the N- or C- terminus. However, any additional amino acids (if present) *do not prevent hTERT sequence fragment from being immunogenic* for a specific response against hTERT, as required by the claims.

Restriction:

Applicants acknowledge with gratitude rejoinder of claims 10, 19, and 21-33 into the group under examination. Applicants also acknowledge with gratitude vacation of the requirement for further restriction within Group 2, and inclusion of claims 25-26 in the elected group.

Applicants responded to the original restriction requirement on September 21, 2004 by electing Group 2 *without traverse*. Applicants does not dispute that the groups restricted in the Action dated July 28, 2004 may be patentably distinct. The request that the Office consider additional claimed subject matter in the examination of this application was made on the basis that the groups could be examined together without undue burden to the Office, and that this would save applicants the trouble and expense of filing divisional applications.

The amended claims now cover subject matter which falls entirely within Group 2. Applicants agree to pursue claims to the other Groups in related applications in this series that have already been filed, or to be filed in the future.

Objections to the claims

Claims 29-32 were objected to for referring to nucleic acid which is a plasmid or a vector. In accordance with the Examiner's suggestion, the claims have now been amended to indicate that the nucleic acid is contained in (and thus a part of) such plasmid or vector. Claim 1 and its dependents have been amended to refer to compositions containing hTERT nucleic acids.

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Rejections under 35 USC § 112 ¶ 1:

The claims under examination stand rejected under the written description requirement of § 112 ¶ 1. The Office Action questions whether there is literal support for the particular sequences and fragment lengths referred to in the claims.

Applicants respectfully remind the Office that the standard for written description under § 112 ¶ 1 need not provide *in haec verba* support for the claimed subject matter. The U.S. courts have long recognized that claim language may be amended in the course of prosecution to improve precision and focus on embodiments which applicants believe to be of commercial importance. We are not bound in this endeavor to slavishly copy language found in the specification as filed. The written description requirement is fully satisfied if the disclosure of the application as originally filed reasonably conveys to the skilled reader that the inventor had possession at the time of filing what is *subsequently claimed* — regardless of whether the ultimate claim language appeared literally in the original disclosure¹.

In the present instance, the application discloses for the first time the protein sequence of human telomerase reverse transcriptase (hTERT). It refers to the use of the protein, fragments thereof as small as 5 amino acids in length, and nucleic acids that encode hTERT and its fragments for a number of purposes, including use in vaccines and for immunizing a mammal with the objective of generating hTERT specific antibody (page 64, lines 20-23). The set of fragments of hTERT includes longer fragments (at least 8, 10, 20, 50, and 100 amino acids up to the full length of the sequence) as a *subset* of the genus of all possible fragments that are 5 amino acids or longer. Since the full length sequence is provided (SEQ. ID NO:2), the skilled reader will not doubt that the inventors had possession of fragments of hTERT of any of these lengths that are useful for the purposes described.

¹ In order to satisfy the written description requirement, the disclosure as originally filed need not provide *in haec verba* support for the claimed subject matter at issue. . . . The requirement is met if 'the disclosure of the application relied upon reasonably conveys to the artisan that the inventor has possession at that time of the later claimed subject matter.' *Lampi Corp. v. American Power Products, Inc.*, 56 USPQ2d 1445 (Fed. Cir. 2000). The written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed. *Union Oil Co. of California v. Atlantic Richfield Co.*, 54 USPQ2d 1227 (Fed. Cir. 2000), citing *In re Gosteli*, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) and *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991).

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Applicants respectfully submit that the claims as presently presented are supported by the specification as filed to the extent required by § 112 ¶ 1.

- Immunogenic peptides and polypeptides having an hTERT sequence, *and vectors encoding such polypeptides* for eliciting an anti-hTERT immune response or for use as a vaccine:
 Described *inter alia* on Page 90, lines 12-18.
- Immunogens comprising 5, 6, 8, 10, 20, 23, 24, 27, 30, and 50 amino acids of TERT
 (Claims 1, 21, and 43):
 Described *inter alia* on Page 18, lines 26-28; page 64, lines 21-29; Example 8 (page 176 ff.); Claims 1, 5, and 8 as originally presented.
- Nucleic acids comprising at least about 25, 60, 100, 200, or 500 bases of hTERT encoding sequences (Claims 39 and 41):
 Described *inter alia* on Page 21, lines 15-18.
- Chimeric molecules for eliciting hTERT antibody comprising an amino acid sequence of hTERT fused to another protein (claim 25):
 Described *inter alia* on Page 64, lines 25-27.
- hTERT compositions without hTERT activity but with immunogenic properties (Claims 43 and 46):
 Described *inter alia* on Page 39, lines 1-11. Assays for hTERT activity: page 42, line 26 ff. Strategy for making hTERT without telomerase activity: page 47, line 25 to page 48, line 7; Examples 1 and 16.

The claims under examination also stand rejected under the enablement requirement of 35 USC § 112 ¶ 1 on the assertion that the skilled reader would not know how to use the invention.

Applicants respectfully disagree. The skilled reader will know that any protein of 1132 amino acids in length will have an abundance of immunogenic epitopes. Thus, the protein, and nucleic acid vectors encoding it, can be used according to standard vaccine technology available at the time to raise an immune response, in order to obtain hTERT-specific antibody, to study reactivity against hTERT expressing cells, or for another purpose. Any subfragment can be used in the same manner, as long as it contains at least one epitope that is immunogenic or can be rendered immunogenic by mixing with an adjuvant or conjugating to another protein such as KLH. Such epitopes can be empirically

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determined without undue experimentation, as described *inter alia* on page 64, lines 15-20 of the application as filed. Support for the claims in the specification as filed is indicated above².

The claims have been reworded in this amendment to facilitate understanding of the claimed invention. The skilled reader will appreciate that the specification as filed both describes and enables what is claimed.

The claims are also rejected under 35 USC § 112 ¶ 1 as containing subject matter which was inadequately described in the specification. The Office Action states that the claims encompass immunogenic compositions comprising a broad genus of polynucleotides incorporating only a portion of SEQ. ID NO:2. The Office Action indicates this is problematic because there is no description of conserved regions which are critical to the structure and function of the claimed genus.

Applicants respectfully disagree for several reasons. First, the specification actually does outline in considerable detail regions of the molecule that are implicated in providing telomerase catalytic activity. A number of motifs are described as conserved between telomerase reverse transcriptase molecules of different species (Page 15).

Secondly, conserved regions of the molecule may be important with respect to preserving enzymatic function of the protein — but the claimed nucleic acids encode immunogenic peptides, which are *not necessarily enzymatically active*. The Office Action does not explain how the presence or absence of conserved regions would affect the immunogenicity of the claimed peptide sequences.

Rejections under 35 USC § 112 ¶ 2:

The claims under examination stand rejected under § 112 ¶ 2 as being indefinite for reading on undefined nucleic acid sequences to which an immune response would also be expected. Of course, the claimed product is selected to raise an antibody response against hTERT protein, not hTERT nucleic acid sequences. Applicants respectfully submit that the claims as currently worded are sufficiently clear and definite to comply with the requirements of § 112 ¶ 2.

² *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997) is referred to in the Office Action as standing for the proposition that a representative number of species needs to be described to support a claim to a genus. In *Lilly*, the patent claimed the cDNA sequence of a particular protein for all mammalian species, but only disclosed the mouse sequence. Thus, the sequence of the human cDNA was covered, even though it was not provided in the disclosure. This is different from what is claimed here, since each one of the claimed peptide sequences is contained in SEQ. ID NO:2. Thus, the skilled reader has all the sequence data she needs to practice the full scope of the claimed invention.

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Double patenting:

Claims 1, 10, 19, and 21-22 stand rejected under the judicially created doctrine of obviousness-type double patenting with respect to claim 1 of U.S. Patent 6,093,809.

Applicants respectfully disagree. Claim 1 of the '809 patent covers a polynucleotide consisting of SEQ. ID NO:1, which is the sequence of telomerase reverse transcriptase of *Euplotes aediculatus* (Cols. 3 & 4). The human TRT sequence is also described in the disclosure (SEQ. ID NO:224), but is not claimed.

Accompanying this response is page 957 of the article "Reverse transcriptase motifs in the catalytic subunit of telomerase" by Lingner et al., Science 1997 Aug 15;277(5328):955-9. Fig. 2 shows that the hTRT protein sequence and the *Euplotes* sequence (Ea_p123) have little in common. Appendix A to this response is a BLAST alignment of the human and *Euplotes* sequences. The longest match is the FFYVTE sequence in the T motif. Thus, there is no sequence of at least 10 amino acids claimed in the '809 patent that falls within the claims of the present application, and double patenting does not apply.

Withdrawal of this rejection is respectfully requested.

Claims 1, 10, 19, 21-22, and 33 stand rejected for obviousness-type double patenting with respect to claims 3, 4, and 8-10 of U.S. Patent 6,261,836.

Without implying any admission that all of the claims of the present application are equally affected by the '836 patent, applicants undertake to file a disclaimer in this or the other patent, or to otherwise address this issue, as appropriate, once the claims are otherwise determined to be in allowable condition.

The Examiner is respectfully reminded that there are other issued and pending applications owned or co-owned by Geron Corp. relating to telomerase reverse transcriptase. These currently include the patents and applications listed in Appendix B, and/or in the accompanying Supplemental Information Disclosure Statement.

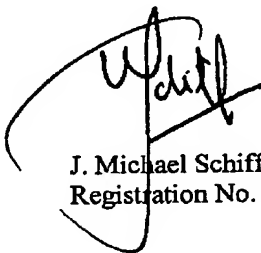
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Fees Due

Enclosed with this Amendment is authorization to charge the Deposit Account for the added claims and the Supplemental Information Disclosure Statement.

Should the Patent Office determine that a further extension of time or any other relief is required for further consideration of this application, applicants hereby petition for such relief, and authorize the Commissioner to charge the cost of such petitions and other fees due in connection with the filing of these papers to Deposit Account No. 07-1139, referencing the docket numbers indicated above.

Respectfully submitted,



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REPORTS

Est2p, but subsequent pairwise comparison of these sequences showed a convincing match. Sequencing of the rest of the cDNA clone containing the EST revealed all eight TRT (Telomerase Reverse Transcriptase) motifs, but not in a single ORF (18). We used the sequence information from this incomplete cDNA clone to isolate an extended cDNA clone from a library of 293 cells, an adenovirus E1-transformed human embryonic kidney cell line (19). This cDNA clone (pGRN121) had a 182-bp insert relative to the EST clone, which increased the spacing between motifs A and B' (18) and put all seven RT motifs and the telomerase-specific motif T motifs in a single contiguous ORF (Fig. 2).

RT-PCR amplification of RNA from 293 cells and from testis each gave two products differing by 182 bp (20). The larger and smaller products from testis RNA were sequenced and found to correspond exactly to pGRN121 and the EST cDNA, respectively..

The relative abundance of hTERT mRNA was assessed in six telomerase-negative mortal cell strains and six telomerase-positive immortal cell lines (21) (Fig. 3). The steady-state level of hTERT mRNA was higher in immortal cell lines with active telomerase (6) than in any of the telomerase-negative cell strains tested. Telomerase activity was more strongly correlated with the abundance of hTERT mRNA than with that of telomerase RNA.

(hTR) (7). In contrast, the abundance of mRNA for the human p80 homolog TP1 (9) did not correlate with telomerase activity (Fig. 3). Thus, while our proposal that hTERT is the catalytic subunit of human telomerase is based mainly on protein structural features

Table 1. Amino acid sequence identity between telomerase reverse transcriptases. Each value is % identity (% similarity in parentheses) based on RT motifs 1, 2, and A through E in Fig 2C.

	hTRT	SpTrt1p	Est2p
Ea p123	26 (49)	28 (45)	24 (46)
Est2p	25 (46)	27 (48)	
SpTrt1p	30 (47)		

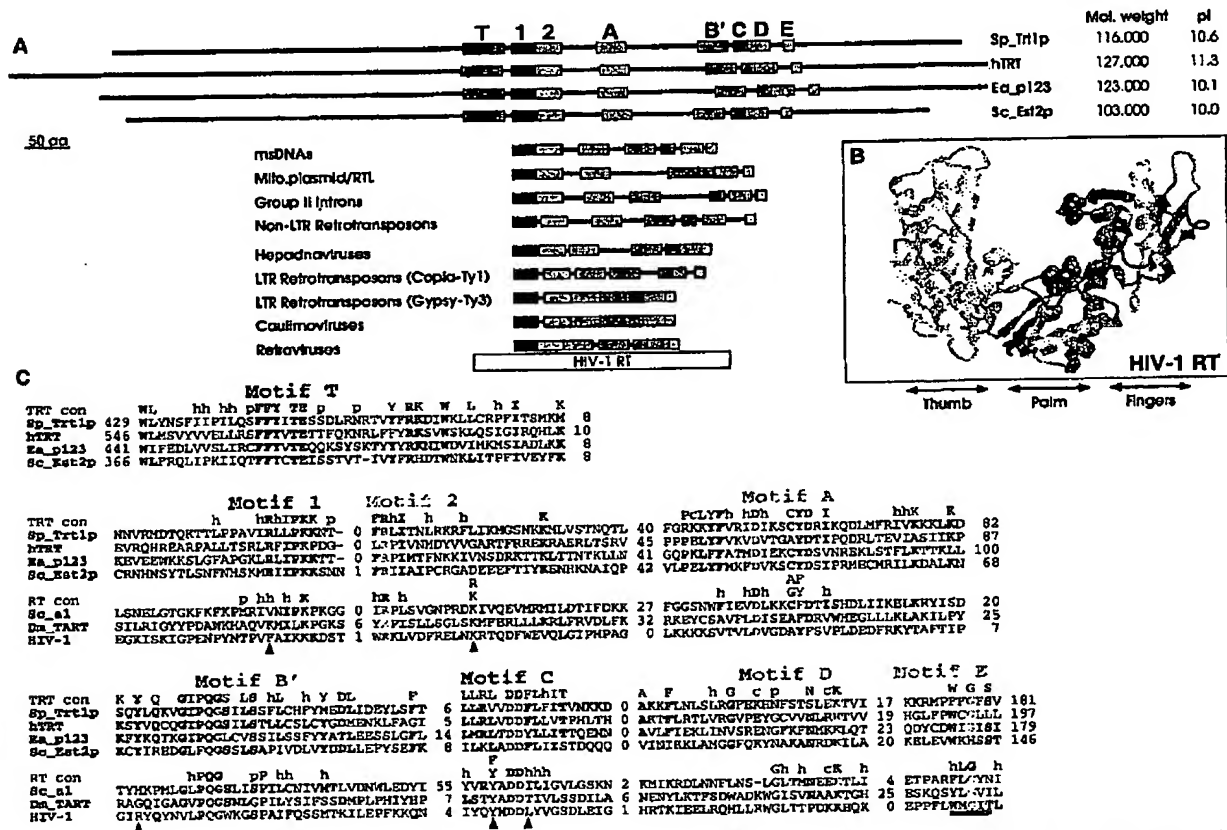


Fig. 2. Structure and RT sequence motifs of telomerase proteins. (A) Locations of telomerase-specific motif T and conserved RT motifs 1, 2, and A through E (24) are indicated by colored boxes. The open rectangle labeled HIV-1 (Human Immunodeficiency Virus) RT delineates the portion of this protein shown in (B). *pl*, isoelectric point. (B) The crystal structure of the p66 subunit of HIV-1 RT (Brookhaven code 1HNV). Color-coding of RT motifs matches that in (A). The view is from the back of the right hand, which allows all motifs to be seen. (C) Multiple sequence alignment of telomerase RTs and members of other RT families (Sc_al, cytochrome oxidase group II, Intron 1-encoded protein from *S. cerevisiae* mitochondria; Dm_TART, reverse transcriptase from *Drosophila melanogaster* TART non-LTR retrotransposable element). Boldface residues indicate identity of at least three telomerase sequences in the alignment. Colored residues are highly con-

served in all RTs and shown as space-filled residues in (B). The number of amino acids between adjacent motifs or to the end of the polypeptide is indicated. TRT con and RT con, consensus sequences for telomerase RTs (this work) and non-telomerase RTs (24) (amino acids are designated h, hydrophobic; A, L, I, V, P, F, W, M; p, polar; G, S, T, Y, C, N, Q; c, charged; D, E, H, K, R). Red arrowheads show some of the systematic differences between telomerase proteins and other RTs. Red rectangle below motif E highlights the primer grip region discussed in the text. Abbreviations for the amino acids are as follows: A, Ala; C, Cys; D, Asp; E, Glu; F, Phe; G, Gly; H, His; I, Ile; K, Lys; L, Leu; M, Met; N, Asn; P, Pro; Q, Gln; R, Arg; S, Ser; T, Thr; V, Val; W, Trp; and Y, Tyr. The nucleotide sequences of the *S. pombe* *trt1+* gene and the human TRT cDNA (pGRN121) have been deposited in GenBank (accession nos. AF015783 and AF015950, respectively).

APPENDIX A: SEQUENCE COMPARISON

Human TERT protein sequence

LOCUS 014746 1132 aa linear PRI 15-JUN-2002
 DEFINITION Telomerase reverse transcriptase (Telomerase catalytic subunit)
 ORGANISM Homo sapiens
 AUTHORS Nakamura,T.M., Morin,G.B., Chapman,K.B., Weinrich,S.L.,
 Andrews,W.H., Lingner,J., Harley,C.B. and Cech,T.R.
 TITLE Telomerase catalytic subunit homologs from fission yeast and human
 JOURNAL Science 277 (5328), 955-959 (1997)

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1 mpraprccrav rsllrshyre vlplatfvrr lgpqgwrlvq rgdpaafra1 vaqclvcvpw
61 darpppaaps frqvscikel varvlqrlce rgaknvlafg falldgargg ppeafttsvr
121 sylpntvtdda lrgsgawgll lrrvgddvlv hllarcalfv lvapscayqv cgpplyqlga
181 atqarpppha sgprrrlgce rawnhsvrea gvplglpapg arrrggsasr slplpkprpr
241 gaapeperpt vggqswahpg rtrgpsdrgf cvvsparpae eatslegals gtrhshpsvg
301 rqhhagppst srpprpwdtp cppvyaetkh flyssgdkeq lrpsfllssl rpsltgarri
361 vetiflgsrp wmpgtprrip rlpqrywqmr plflellgnh aqcpygvlk thcplraavt
421 paagvcarek pggsvaapee edtdprrlvq lrrqhsppwq vygfvracir rlvppglwgs
481 rhnerrflrn tkkfislghk aklsiqeltw kmsvrdcawl rrspgvgcvp aaehrleei
541 lakflhlwms yvvvellrsf fyvtettfqk nrlffyrksv wsklqsigir qhlkrvqlre
601 lseaevrqhr earpalltsr lrfipkpdgl rpivnmdyvv gartfrrekr aerltsrvka
661 lfsvinyera rrpqllgasv lglddihrav rtfvlrvraq dppelyfvk vdvtagydti
721 pqdrltevia siikpntyc vrryavvqka ahghvrkafk shvstltdlq pymrqfvahl
781 qetsplrdav vieqssslne assglfdvfl rfmchhavri rgksyvqcqg ipqgsilstl
841 lcslycydme nklfaglrdd glllrldvdf llvtphltha ktflrtlvrq vpeygcvvnl
901 rktvvnfpye dealggtafv qmpahglfpw cgllldtrtl evqsdysyia rtsirasltf
961 nrgfkagrnrm rrlfvgvlrl kchslfldlq vnsldtvtctn iykillllqay rfhacvllqpl
1021 fhqqvwknpt fflrvisdta slcysilkak nagmslgakg aagplpseav qwlchqefll
1081 kltrhrvtvy pllgslrtaq tqlsrkllpgt tlataleaaan palpsdfkti ld

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Euplotes aediculatus

LOCUS AAC47515 1031 aa linear INV 05-MAY-1997
 DEFINITION telomerase subunit p123 [Euplotes aediculatus].
 ORGANISM Euplotes aediculatus
 REFERENCE 1 (residues 1 to 1031)
 AUTHORS Lingner,J., Hughes,T.R., Shevchenko,A., Mann,M., Lundblad,V. and
 Cech,T.R.
 TITLE Reverse transcriptase motifs in the catalytic subunit of telomerase
 JOURNAL Science 276 (5312), 561-567 (1997)
 PUBMED 9110970

CDS 1..1031
 /coded_by="U95964.1:101..3196"
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ORIGIN

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1 mevdvndqad nhgihsalkt ceeikeaktl yswlqkvirc rnqsqshyk dledikifaqt
61 nivatprdyn eedfkvlark evfstglmie lidkclvell sssdvsdrqk lqcqfqlkg
121 nqlakthllt alstqkqyff qdewnqvram ignelfrhly tkylifqrts egtlvqfcgn
181 nvfdhikvnd kfdkkqkgga admneprccs tckynvknec dhflnninvp nwnnmksrtr
241 ifycthfnnr nqffkkhefv snknnisamd raqtiftnif rfnrirkklk dkviekiaym
301 lekvdnfnnr yyltkscplp enwrerkqki enlinktree kskyeeelfs yttndkcvrtq
361 fineffynil pkdfltgrrn knfkqkvkky veinkhelih knlilekint reiswmqvte
421 sakhfyyfdh eniyvlwkl1 rwifedlvvs lircffyvte qqksysktyy yrkniwdvim
481 kmsiadlkke tlaevqekev eewkkslgfa pgklrlipkk ttfripimtfn kkivnsdrkt
541 tkltntnkl1 nshlmkltk1 nrmfkdpgf avfnyddvmk kyeevfckwk qvgqpk1ffa
601 tmdiekcyds vnreklstfl kttklssdf wintaqilkr knnividskn frkkmkdyf
661 rdkfkqiale ggqyptlfsv leneqndlna kktliveakq rnyfkddnll qpvinicqyn
721 yinfngkfyk qtkgipqglc vssilssfy atleesslgf lrdesmnpn prvnllmrlt
781 ddyllittqe nnavlfiek1 invsrengfk fnmkkllqtsf plspskfaky gmdsveeqni

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841 vqdycdwigi sidmktlalm pninlriegi lctlnlnmqt kkasmwlkkk lksflmnnit
 901 hyfrktitte dfanktlinkl fisggykymq cakeykdhfk knlamssmid levskiiysv
 961 traffkylvc nikdtifgee hypdfllstl khfielfstk kyifnrvcmf lkakeaklks
 1021 dqcqsligyd a

BLAST COMPARISON

Source: <http://www.ncbi.nlm.nih.gov/blast/bl2seq/wblast2.cgi>

Human:	464	FVRACLRRLVPPGLWGSRHNERRFLNRTKKFISLGKHAKLSLQELTWKMSVRDCAWLRRS	523
		F+ ++P R N + F + KK++ L KH + L K++ R+ +W++	
Eup1A:	361	FINEFFYNILPKDFTLGR-NRKNFQKKVKYVELNKHელიHKNLLEKINTREISWMQVE	419
Human:	524	PGVGCVPAAEHLREEILAKFLHWMMSVYVVELLRSEFFVVTETTFQKNRLFFYRKSVWSK	583
		+H +L K L W+ VV L+R GGVIG ++ ++YRK++W	
Eup1A:	420	TSAKHFYYFDHE-NIYVLWKLRLWIFEDLVVSLIRCFYVTEQQKSYSKTYYYRKNIDV	478
Human:	584	LQSIGIRQHLKRVQLRELSEAEVROHREARPALTSRLRFIPKPDGLRPTVNMDYVVGAR	643
		+ + I LK+ L E+ E EV + +++ +LR IPK RPI+ + +	
Eup1A:	479	IMKMSIAD-LKKETLAEVQEKEVEEWKSL-GFAPGKLRLLIPKKTFRPIMTFN----	532
Human:	644	TFRREKRAERLTSRVKALFVSLNYERARR---PGLLGASVLGLDDIHRWRTFVLRVRAQ	700
		+++ +LT+ K L S L + + G +V DD+ + + FV + + Q	
Eup1A:	533	IVNSDRKTTKLTNTKLLNSHMLKLTKNRMFKDPFGFAVFNYYDDVMKKYEEFVCKWK-Q	591
Human:	701	DPPPELYFVKVDVTGAYDTIPQDRLTEVI-----ASIIKPQNTYCYVRRYAV	746
		P+L+F +D+ YD++ +++L+ + A I+K +N +	
Eup1A:	592	VGQPKLFFATMDIEKCYDSVNREKLTSTFLKTTKLLSSDFWINTAQILKRNKNIVDSKNF	651
Human:	747	VQKAAHGHVVRKAFKSHYSTLTDLQPYMRQFVAHLQETSPLRDAVVIEQSSSLNEASSGLF	806
		+K + R+ F+ ++ P + + + Q + +++E L	
Eup1A:	652	RKKEMKDYFRQKFQK-IALEGGQYPTLFSVLENEQNOLNAKKTLLIVEAKQRNYFKKDNLL	710
Human:	807	DVFLRFMCHHAVRIRGKSYVQCQGIPOGSILSTLLCSLCYGD MENKLFAGIRRD-----	860
		+ ++ + GK Y Q + GIPGG +S++L S Y +E +R +	
Eup1A:	711	QPVINICQYNYINFNGKFKYKQTKGIPQGLCVSSILSSFYATLEESSLGFLRDESMNPEN	770
Human:	861	---GLLLRLVDDFLLVTPHLTHAKTFLRTLVRGVPEYGCVVNLKRTVNVNFPVEALGGT	917
		LL+RL DD+LL+T +A F+ L+ E G N++K +FP+	
Eup1A:	771	PNVNLLMRLTDYLLITTQENNAVLFIKLLINSRENGFKFNMKKLQTSFPLSPSKFAKY	830
Human:	918	AFVQMPAHGLF----PWCGLLLDTRTLEQSDYSSYARTSIRASLTFRNGFKAGRNMRRK	973
		+ + W G+ +D +TL + + + I +L N K +K	
Eup1A:	831	GMDSVEEQNTIVQDYCDWIGISIDMKTALMPNINLRIE-GILCTLNLMQTKKASMWLKK	889
Human:	974	LFGVRLRLKCHSLFLDLQVNSLQTVCTNIYKILLQAYRFHACVQLQPFHQVWKNPTFFL	1033
		+ + + + + K+ + Y++ C + H + KN	
Eup1A:	890	KLKSFLMNNITHYFRKTITTEDFANKTLNKLFISSGGYKYMQCAKEYKDHFK--KNLAMSS	947
Human:	1034	RVISDTASLCYSILKA	1049
		+ + + + YS+ +A	
Eup1A:	948	MIDLEVSKIISVTRA	963

APPENDIX B: OTHER PATENTS AND APPLICATIONS

Recombinant hTERT	U.S. Patent 6,475,789; U.S. Patent 6,261,836; U.S. Patent 6,617,110; U.S. Patent 6,808,880; U.S. Patent 6,921,664; U.S. Patent 6,927,285; USSN 09/843,676 (allowed); USSN 10/054,611 (allowed); USSN 08/974,584; USSN 09/432,503; USSN 09/721,477; USSN 09/721,506; USSN 10/053,758; USSN 10/044,692; USSN 10/877,022; USSN 10/877,124; USSN 10/044,539; USSN 10/877,146; Continuation of 09/721,477 filed on about August 17, 2005
hTERT variants	U.S. Patent 6,337,200; USSN 09/990,080
TRT from single cell ciliates	U.S. Patent 6,093,809; U.S. Patent 6,166,178; U.S. Patent 6,309,867
Mouse TRT	U.S. Patent 6,767,719; USSN 10/862,698
Telomerase holoenzyme purified from cells having telomerase activity	U.S. Patent 5,968,506; U.S. Patent 6,261,556; U.S. Patent 6,517,834; U.S. Patent 6,545,133; U.S. Patent 6,787,133; USSN 10/811,033
Use of recombinant hTERT in vaccine formulations	U.S. Patent 6,440,735; USSN 10/208,243; USSN 10/602,441
hTERT promoter	U.S. Patent 6,610,839; U.S. Patent 6,777,203; USSN 10/325,810; USSN 10/674,836
hTERT antisense oligonucleotides	U.S. Patent 6,444,650; U.S. Patent 6,627,619; USSN 10/637,443